

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
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## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference <b>68103-PCT/JPW/JL</b>		Date of mailing (day/month/year) <b>18 AUG 2003</b>
International application No. <b>PCT/US04/36781</b>		FOR FURTHER ACTION See paragraph 2 below
International filing date (day/month/year) <b>05 November 2004 (05.11.2004)</b>	Priority date (day/month/year) <b>07 November 2003 (07.11.2003)</b>	
International Patent Classification (IPC) or both national classification and IPC <b>IPC(7): C12Q 1/68, 1/02, 1/34; C07K 14/00 and US Cl.: 435/6, 29, 18; 530/350</b>		
Applicant <b>THE TRUSTEES OF COLUMBIA UNIVERSITY IN NYC</b>		

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I      Basis of the opinion
- ☐ Box No. II      Priority
- ☒ Box No. III      Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV      Lack of unity of invention
- ☒ Box No. V      Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI      Certain documents cited
- ☐ Box No. VII      Certain defects in the international application
- ☒ Box No. VIII      Certain observations on the international application

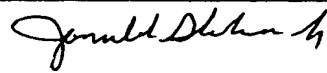
**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Jennifer Dunston  Telephone No. 571-272-0507
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Form PCT/ISA/237 (cover sheet) (January 2004)

Applicants: Kausik Si and Eric Kandel  
U.S. Serial No. NOT YET KNOWN  
Filed: Herewith (as §371 national stage  
of PCT/US2004/036781)  
**Exhibit 6**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/US04/36781

**Box No. I Basis of this opinion**

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing  
☐ contained in international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/36781

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

I. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 2 and 15

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 2 and 15 will not be examined because sequence identifiers were not provided and no sequence listing was provided, are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. \_\_\_\_\_

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐

has not been furnished

☐

does not comply with the standard

the computer readable form

☐

has not been furnished

☐

does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US04/36781

**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims <u>1, 3-14, 16-36 and 40-43</u>	YES
	Claims <u>37-39</u>	NO
Inventive step (IS)	Claims <u>1, 3-14, 16-36 and 40-43</u>	YES
	Claims <u>37-39</u>	NO
Industrial applicability (IA)	Claims <u>1, 3-14 and 16-43</u>	YES
	Claims <u>NONE</u>	NO

**2. Citations and explanations:**

Claims 37-39 lack novelty under PCT Article 33(2) as being anticipated by Liu et al. Liu et al teach the neuronal isoform of the Aplysia CPEB protein comprising a glutamine-rich region near the N-terminus (e.g. paragraph bridging pages 71-72; Figure 4). The ability of the protein to form a prion is an inherent property of the neuronal isoform of Aplysia CPEB. Thus, Liu et al necessarily teach the claimed isolated prion form of the Aplysia CPEB protein.

Claims 1, 3-14, 16-36 and 40-43 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest that cytoplasmic polyadenylation element binding protein is capable of forming a prion, whereby the aggregated form is the active form capable of activating translation of a transcript comprising a cytoplasmic polyadenylation element.

Claims 1, 3-14 and 16-43 the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

**WRITTEN OPINION OF THE  
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International application No.

PCT/US04/36781

**Box No. VIII Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claims 40 and 41 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because the claims are not fully supported by the description. The application, as originally filed, did not describe any agent that facilitates the conversion of a cytoplasmic polyadenylation element binding protein between the prion and non-prion forms. Although the specification describes a method for identifying such agents, the specification fails to provide adequate written description and evidence of possession of a claimed genus of agents. The specification does not provide sufficient distinguishing identifying characteristics of the genus. The specification does not describe a complete or partial structure, for any agent. Therefore, the specification does not provide adequate written description for the claimed genus of agents.

Claims 40-43 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because the claims are not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because: the specification does not describe a partial or complete structure for any agent capable of converting a cytoplasmic polyadenylation element binding protein (CPEB) between its prion and non-prion form and does not teach how to make an agent capable of performing the claimed function. Although the specification teaches the step of identifying an agent that facilitates the conversion of CPEB between prion and non-prion forms, the screening method used to identify the agents does not provide any guidance for the manufacture of the agents. The specification lacks teachings with regard to how to make the claimed agent and lacks guidance with regard to any structural features of the agents, which would allow one of skill in the art to make the claimed agent. Therefore, claims 40-43 are not considered to be enabled by the instant specification.